

Supplementary material: 1

## **Methods**

### **Questionnaires and neuropsychological measures**

#### **Barratt Impulsiveness Scale 11th version (BIS-11)**

Subjects were administered the Chinese version of the BIS-II, a validated 30-item questionnaire that measures different dimensions of impulsivity (16). The BIS-II contains three subscales: attention impulsiveness (e.g., “I get easily bored when solving thought problems”), motor impulsiveness (e.g., “I am restless at the theater or lectures”) and non-planning impulsiveness (e.g., “I spend or charge more than I earn”). The Chinese version of the BIS-II has been shown to have good internal consistency and test-retest reliability.

#### **Working memory (digit-span test)**

Working memory was assessed using the digit-span test (17), which has two subtests: forward (simple attention) and backward (concentration, complex attention). Participants are asked to repeat increasingly long strings of digits that are read to them by an examiner. On the forward subtest, participants simply repeat the strings until they fail to repeat an entire trial (composed of two strings of identical length) correctly. On the backward subtest, participants are required to repeat the digit string in the reverse order

until they fail both strings in a trial. Outcome was expressed in terms of number of digits forward achieved and number of digits backward achieved.

### **d2 test of attention/psychomotor speed**

From a series of the letters d and p, with one or two lines above and/or below each letter, the participants were asked to mark the d's with two lines as quickly and accurately as possible. A summary test score was calculated using the number of correctly marked d's minus the number of errors (18).

## **Results**

### **Decision-making performance in former heroin addicts at different abstinent times**

#### **Demographic and clinical characteristics of subjects**

The demographic and substance-abuse characteristics of the subjects are summarized in Table 1. One-way ANOVA showed a significant effect of Group on anxiety [ $F(8,174)=18.37, p<0.05$ ]; pairwise comparisons showed significant differences between the healthy control group and each of the short-term abstinence groups (3 d, 7 d, 15 d, 30 d) (all  $p$  values $<0.05$ ). There was a significant group effect on self-report ratings of

depression on the BDI-II [ $F(8,173) = 9.15, p < 0.05$ ], pairwise comparisons showed significant differences between the healthy control group and each of the groups of former heroin addicts (all  $p$  values  $< 0.05$ ). There were no significant group differences in age, education, digit span, the d2 test of attention. And drug-use history (duration and dose) was not significantly different among the groups of former addicts.

#### Self-reported impulsivity on the BIS-II

Table 2 shows self-reported impulsivity on the BIS-II in healthy controls and former heroin addicts. There was a significant main effect of Group on motor impulsiveness [ $F(8,174) = 2.15, p < 0.05$ ], non-planning impulsiveness [ $F(8,174) = 3.14, p < 0.05$ ], and total score [ $F(8,174) = 3.39, p < 0.05$ ]. However, none of the pairwise comparisons was significant.

#### Effects of stress on decision-making deficits in abstinent heroin addicts

##### Demographic and clinical characteristics of subjects

The demographic and substance-abuse characteristics of the subjects are summarized in Table 3. There was a significant effect of Group on anxiety [ $F(5,117) = 13.83, p < 0.05$ ]; in pairwise comparisons, healthy controls differed from each of the short-term abstinence groups (15 d, 30 d) (both  $p$  values  $< 0.05$ ). There was also a significant effect of Group on depression on the BDI-II [ $F(5,117) = 15.29, p < 0.05$ ]; pairwise comparisons showed that healthy controls differed from each of the heroin groups (all  $p$  values  $< 0.05$ ). There were no significant group differences in age,

education, digit span, or the d2 test of attention. There were also no significant differences among the former addicts in terms of drug-use history (duration and dose).

#### Self-reported impulsivity on the BIS-II

Table 4 shows self-reported impulsivity on BIS-II in heroin addicts and healthy controls. There was a significant effect of Group on motor impulsiveness [ $F(5,117) = 3.50, p < 0.05$ ], non-planning impulsiveness [ $F(5,117) = 3.19, p < 0.05$ ], and total score [ $F(5,117) = 5.16, p < 0.05$ ]; however, none of the pairwise comparisons reached significance.

#### **Effects of propranolol on stress-induced exacerbation of decision-making deficits in former heroin addicts**

##### Demographic and clinical characteristics of subjects

Former heroin addicts who had been abstinent for 30 d (n=41), 12 m (n=40), and 24 m (n=37) were enrolled and completed the study. Their demographic and substance-abuse characteristics are summarized in Table 5. One-way ANOVA showed no significant group differences in age, education, drug-use history (duration and dose), anxiety score, depression score, digit span, or the d2 test of attention.

##### Self-reported impulsivity on the BIS-II

Table 6 shows self-reported impulsivity on BIS-II in the former heroin addicts. There was no effect of Group on any of the subscales or the

total score ( $p > 0.05$ )

**TABLE S1: Demographic and clinical characteristics of participants in Experiment 1**

Characteristic	Control (n=21)	3 d (n=18)	7 d (n=19)	15 d (n=18)	30 d (n=20)	3 m (n=19)	6 m (n=19)	12 m (n=21 )	24 m (n=20 )	<i>p</i> value
Age(years)	30.19±4.33	32.33±4.99	29.44±4.67	31.94±6.01	30.60±6.20	30.74±6.11	32.74±6.10	32.24±5.21	30.95±6.23	0.53
Education(years)	10.71±1.82	9.56±2.18	9.22±1.93	9.94±3.12	8.78±3.11	9.47±2.29	9.34±1.92	9.52±2.58	9.45±1.19	0.36
Duration of heroin use (years)		6.99±4.68	7.55±3.83	7.87±3.50	6.79±4.58	7.88±4.03	8.00±3.36	7.32±3.79	8.11±3.58	0.95
Average dose(g)		0.86±0.56	0.87±0.73	0.98±0.63	0.93±0.78	0.83±0.60	0.81±0.75	0.80±0.44	0.91±0.54	0.99
HAMA Score	2.57±1.47	11.83±3.52*	7.50±4.53*	8.56±4.60*	5.60±2.89*	3.63±1.74	4.37±1.42	4.00±3.02	3.30±2.92	0.001
BDI-II Score	3.90±1.92	17.06±7.27*	15.61±7.98*	15.44±5.27*	13.15±6.78*	10.42±5.18*	11.44±5.94*	13.48±5.48*	9.60±5.49*	0.001
Working memory										
Forward condition	8.07±0.86	8.06±0.80	8.09±1.04	8.06±0.64	8.05±1.05	8.05±1.03	7.84±1.30	7.57±1.17	7.65±0.93	0.22
Backward condition	6.02±1.12	5.83±1.29	5.67±1.19	5.67±1.61	5.40±1.28	5.42±0.77	5.74±1.52	5.00±1.38	5.40±1.43	0.12
D2 test of attention	195.40±34.51	176.06±60.09	184.94±35.35	180.35±47.69	177.40±39.81	176.58±27.46	176.58±38.04	175.81±34.01	173.29±30.11	0.77

Values are shown as mean±SD. No group differences were found in age, education, working memory, or the d2 test of attention. Among the former heroin addicts, no group differences were found in heroin-abuse characteristics (duration and dose). \**p* <0.05, significant difference between former heroin addicts and healthy controls.

**TABLE S2: Self-reported impulsivity on the BIS-II in former heroin addicts and healthy controls in Experiment 1**

Scale/subscale	Control (n=21)	3 d (n=18)	7 d (n=19)	15 d (n=18)	30 d (n=20)	3 m (n=19)	6 m (n=19)	12 m (n=21 )	24 m (n=20 )	<i>p</i> value
BIS- Attention	16.48±2.87	17.72±2.68	17.72±2.35	17.00±2.28	18.75±2.16	17.05±2.74	18.11±3.05	18.11±3.05	17.00±3.58	0.25
BIS -Motor	22.67±3.40	26.44±4.57	26.78±3.14	25.17±3.33	27.10±5.24	26.40±5.35	24.84±3.40	24.84±3.40	25.60±3.83	0.03
BIS- Non-planning	23.81±4.67	27.72±7.33	28.33±4.12	28.06±5.37	28.50±5.51	29.60±3.66	30.47±3.81	30.47±3.81	27.95±4.17	0.002
BIS- Total	62.86±6.35	71.33±10.54	72.94±7.52	70.44±9.39	73.80±8.36	73.16±8.64	73.42±7.23	73.42±7.23	70.55±9.39	0.001

Values are shown as means ±SD. Among the former heroin addicts, no group differences were found in Attention, Motor, Non-planning, or Total scores.

**TABLE S3: Demographic and clinical characteristics of subjects in Experiment 2**

Characteristic	Control (n=20)	15 d (n=18)	30 d (n=23)	3 m (n=20)	12 m (n=19)	24 m (n=18)	p value
Age(years)	29.95±4.96	31.94±6.01	29.78±7.07	31.85±4.65	32.47±4.68	30.33±6.32	0.53
Education(years)	10.40±1.39	9.94±3.11	9.61±1.99	10.35±1.84	9.74±2.58	9.67±1.37	0.74
Time of heroin use (years)		8.25±4.09	7.73±3.48	8.16±3.43	8.09±3.3	8.04±3.68	0.99
Average dose		1.15±0.88	1.02±0.70	1.06±0.61	0.89±0.39	0.95±0.56	0.78
HAMA Score	2.25±1.55	8.56±4.60*	4.52±2.63*	3.38±1.61	3.45±1.67	2.61±2.43	0.001
BDI- II Score	3.95±1.93	15.44±5.27*	15.04±6.09*	9.68±5.13*	10.89±3.35*	9.17±5.79*	0.001
Working memory							
Forward condition	7.80±0.95	8.06±0.64	7.48±0.95	7.75±1.07	7.84±1.01	7.68±0.97	0.17
Backward condition	5.80±1.15	5.67±1.61	5.04±1.07	5.30±1.34	5.26±1.37	5.33±1.41	0.14
D2 test of attention	197.90±37.98	177.78±47.54	176.70±50.85	183.55±47.00	174.05±34.77	173.33±33.89	0.47

Values are shown as mean± SD. No significant group differences were found in age, education, working memory, or the D2 test of attention. Among the former heroin addicts, no group differences were found in heroin-abuse characteristics (duration and dose). \* $p < 0.05$ , significant difference between former heroin addicts and healthy controls.



**TABLE S4: Self-reported impulsivity on the BIS-II in former heroin addicts and healthy control in Experiment 2**

Scale/subscale	Control (n=20)	15 d (n=18)	30 d(n=23)	3 m (n=20)	12 m (n=19)	24 m (n=18)	p value
BIS- attention	16.20±3.14	17.00±2.28	16.65±3.88	16.68±3.27	17.37±2.54	15.89±3.20	0.24
BIS -Motor	22.30±3.86	25.17±3.33	27.09±4.73	25.45±3.35	25.84±2.87	25.11±4.46	0.01
BIS- Non-planning	24.50±4.35	28.06±5.37	29.70±4.68	29.00±3.53	27.58±5.15	27.89±4.27	0.00
BIS- Total	63.00±6.66	70.44±9.39	76.00±10.32	73.32±7.61	70.79±7.89	68.89±10.40	0.00

Values are shown as means±SD. Among the former heroin addicts, no group differences were found in Attention, Motor, Non-planning, or Total scores.

**TABLE S5: Demographic and clinical characteristics of subjects in Experiment 3**

Characteristic	30 d groups		12 m groups		24 m groups		<i>p</i> value
	placebo (n=20)	propranolol (n=21)	placebo (n=19)	propranolol (n=21)	placebo (n=19)	propranolol (n=18)	
Age	30.75±6.87	32.10±6.53	32.26±5.50	31.33±6.47	34.16±5.61	32.33±5.94	0.64
Education	8.10±1.71	8.10±1.70	8.47±1.50	8.57±1.72	8.37±1.91	8.61±1.94	0.89
Time of heroin use	7.64±3.59	7.69±5.24	8.05±4.36	7.89±4.92	7.73±3.71	7.58±3.87	0.90
Average dose	1.05±0.73	0.83±0.82	0.75±0.45	0.61±0.53	0.69±0.40	0.81±0.46	0.28
HAMA Score	4.30±2.36	4.24±3.83	5.84±3.00	4.81±2.96	5.89±3.50	5.44±3.67	0.39
BDI- II Score	15.65±6.21*	14.75±7.79*	12.52±6.16	11.62±7.64	9.16±4.00	10.56±7.96	0.03
Working memory							
Forward condition	7.24±0.83	7.24±0.89	7.21±0.92	6.87±0.85	7.37±1.37	7.06±1.06	0.66
Backward condition	4.45±0.60	4.24±0.54	4.32±0.82	4.62±0.80	4.95±1.13	4.94±1.06	0.18
D2 test of attention	174.20±45.23	163.48±21.95	163.79±21.90	169.90±30.73	169.21±26.04	173.67±30.53	0.82

Values are shown as means±SD. No group differences were found in age, education, heroin-abuse characteristics (duration and dose), HAMA Score, digit span, or the D2 test of attention. \**p* <0.05, significant difference between 30 d group and 12 m, 24 m groups.

**TABLE S6: Self-reported impulsivity on the BIS-II in former heroin addicts in Experiment 3**

Scale/subscale	30 d groups		12 m groups		24 m groups		<i>p</i> value
	placebo (n=20)	propranolol (n=21)	placebo (n=19)	propranolol (n=21)	placebo (n=19)	propranolol (n=18)	
BIS- Attention	17.90±3.75	17.00±2.35	16.32±4.23	17.48±2.34	18.05±1.77	16.33±2.89	0.23
BIS –Motor	27.05±4.91	25.86±3.72	26.53±4.14	26.62±5.02	24.00±3.28	25.06±5.23	0.28
BIS- NP	29.50±4.97	28.81±3.83	29.59±3.99	27.81±4.29	26.74±4.19	27.22±4.97	0.13
BIS- Total	74.45±11.01	72.19±6.61	71.95±6.96	72.28±7.52	69.68±5.20	68.83±11.27	0.18

Values are shown as means±SD. No significant group differences were found in Attention, Motor, Non-planning and Total scores.

Figure S1 shows effects of stress on diastolic pressure in former heroin addicts who had been abstinent for 15 d, 30 d, 3 m, 12 m, or 24 m, and healthy controls. Three-way repeated-measure ANOVA showed no significant interaction of Stress X Time ( $[F(1,336) = 3.7, p = 0.0553]$ ).

Figure S2 shows effects of propranolol on diastolic pressure in former heroin addicts who had been abstinent for 30 d, 12 m, or 24 m. Four-way repeated-measure ANOVA showed no significant interaction of Time X Stress X Propranolol or and Time X Stress ( $[F(3,336) = 1.52, p = 0.2104]$ ;  $[F(1,336) = 1.03, p = 0.3115]$ ).

Fig s1: Effects of stress on diastolic pressure in the former heroin addicts.

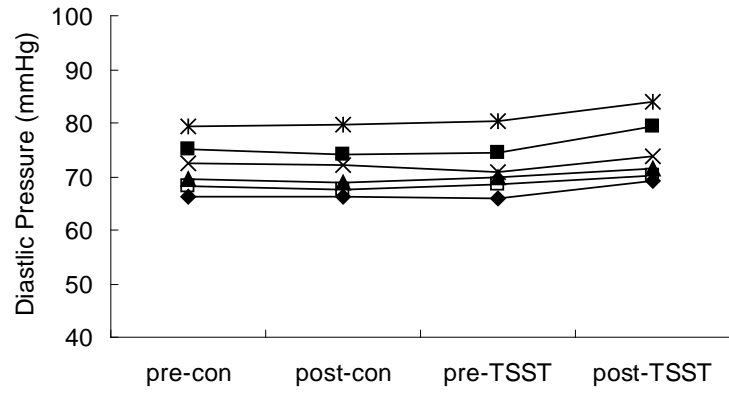


Fig s2: Effects of propranolol on diastolic pressure in the former heroin addicts.

